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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/555,964	09/08/2000	Meir Shinitzky	24259	9351

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EXAMINER	
HUYNH, PHUONG N	

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1644	19

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/555,964	Applicant(s) SHINITZKY ET AL.	
	Examiner Phuong Huynh	Art Unit 1644	

-- The MAILING DATE of this communication app ars on the cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/11/03 has been entered.

2. Claims 6-13 are pending and are being acted upon in this Office Action.

3. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 6-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for:

(1) A method for the preparation of a reagent for use in diagnosis of schizophrenia in an individual by detecting a DTH reaction in said individual following injection of said reagent to the individual, comprising: (a) obtaining blood samples from a number of individual, preparing a pool from said samples and collecting platelets therefrom; (b) preparing a protein fraction from said platelet preparation comprising proteins or fractions thereof having a pI in the range of 6.5 to 9.5;

(2) A diagnostic method for determining schizophrenia in a subject comprising: (a) obtaining a blood samples from a subject and collecting platelets therefrom, (b) injecting said platelets into a subject and (c) examining the subject for the occurrence of delayed type hypersensitivity reaction at the site of injection, a positive result being a reaction above that which is observed in non-schizophrenic subject, indicating that the subject has a high likelihood of being schizophrenic;

(3) A method for the preparation of a reagent for use in diagnosis of schizophrenia in an individual by detecting a DTH reaction in said individual following injection of said reagent to the individual comprising: (a) obtaining blood samples from a number of schizophrenic or non-schizophrenic individuals, preparing a pool from said samples and collecting platelets therefrom; (b) preparing a protein fraction from said platelet preparation comprising proteins or fractions thereof having a pI in the range of 6.5 to 9.5, (c) injecting said protein preparation into a subject and (d) examining the subject for the occurrence of delayed type hypersensitivity reaction at the site of injection, a positive result being a reaction above that which is observed in non-schizophrenic subject, indicating that the subject has a high likelihood of being schizophrenic;

(4) A method for the preparation of a reagent for use in diagnosis of schizophrenia in an individual by detecting a DTH reaction in said individual following injection of said reagent to the individual comprising: (a) obtaining blood samples from an individuals and collecting platelets therefrom; (b) preparing a protein fraction therefrom from said platelet preparation comprising proteins or fractions thereof having a pI in the range of 6.5 to 9.5, (c) injecting said protein preparation into a subject and (d) examining the subject for the occurrence of delayed type hypersensitivity reaction at the site of injection, a positive result being a reaction above that which is observed in non-schizophrenic subject, indicating that the subject has a high likelihood of being schizophrenic, **does not** reasonably provide enablement for *any* methods as set forth in claims 6-13 for diagnosis of schizophrenia in an individual. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only a diagnostic method for determining schizophrenia in a subject comprising the steps of obtaining blood sample from a subject, preparing a pool of platelets from said subject, injecting said platelets or a proteins fraction from platelet having a pI

in the range of 6.5 to 9.5 into a subject and examining the subject for the occurrence of delayed type hypersensitivity reaction at the site of the injection, a positive result being a reaction above that which is observed in non-schizophrenic subjects, indicating that the subject has a high likelihood of being schizophrenic.

The specification does not teach how to make and use *any* platelet proteins or fractions therefrom "having a pI of above about 6.5" for a diagnostic method of schizophrenia in a subject because the term "having" is open-ended. It expands the range of the pI at either or both ends of the platelet proteins or platelet protein fraction. In fact, the specification discloses that platelet proteins having a pI in the range of 2 to 6.5, referenced as pool 1, has no DTH response in schizophrenic patient (See page 13). Not only there are more than one platelet proteins associated with any one specific pI, there is insufficient guidance as to the molecular weight of any platelet proteins associated with that particular pI, let alone the structure associated with function of any platelet proteins for the claimed diagnostic method. A platelet protein without the molecular weight associated with the specific amino acid sequence has no structure, much less function.

Stryer *et al* teach that a protein is highly dependent on the overall structure of the protein itself and that the primary amino acid sequence determines the conformational of the protein (See enclosed appropriate pages).

Applicants have not provided any biochemical information (e.g. molecular weight, amino acid composition, N-terminal sequence, etc.) that distinctly identifies the various platelet proteins for the claimed method. While protein having a range of pI of above about 6.5 or a pI within the range of above 6.5 to about 9.5 may have some notion of the activity such as induces DTH, claiming a method of injecting platelet proteins fails to distinctly claim what that proteins are and what the compositions are made up of for the claimed method. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. The specification does not describe nor enable any platelet proteins for the claimed diagnostic method other than the isolated platelet or platelet proteins fraction having a pI in the range of 6.5 to 9.5 as disclosed on page 12 of the specification.

Given the indefinite number of undisclosed platelet proteins having a pI of above about 6.5 or within the range of above 6.5 to about 9.5, it is unpredictable which undisclosed platelet proteins is useful for the claimed method of diagnosing schizophrenia in a subject. Therefore, it would require undue experimentation of one skilled in the art to practice the claimed invention.

See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

6. Claims 6-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of *any* methods as set forth in claims 6-13 for diagnosis of schizophrenia in an individual.

The specification discloses only a diagnostic method for determining schizophrenia in a subject comprising the steps of obtaining blood sample from a subject, preparing a pool of platelets from said subject, injecting said platelets or a proteins fraction from platelet having a pI in the range of 6.5 to 9.5 into a subject and examining the subject for the occurrence of delayed type hypersensitivity reaction at the site of the injection, a positive result being a reaction above that which is observed in non-schizophrenic subjects, indicating that the subject has a high likelihood of being schizophrenic.

With the exception of the specific isolated platelet or platelet proteins fraction having a pI in the range of 6.5 to 9.5 for the claimed diagnostic method, there is insufficient written description about the structure associated with function of *any* platelet proteins having a pI of about 6.5, *any* platelet protein fraction having a pI of about 6.5, *any* platelet proteins have a pI within the range of above 6.5 to about 9.5 because there is written description about the structure associated with function such of any platelet proteins such as the molecular weight, amino acid composition, N-terminal sequence that distinctly identifies the various platelet proteins with that particular pI in the protein fraction for the claimed method of diagnosis of schizophrenia in an individual.

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

8. Claims 6, 7 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The "having a pI **above about** 6.5" in claims 6, 7 and 9 is indefinite and ambiguous. One of ordinary skill in the art cannot appraise the metes and bounds of the claimed invention.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 6-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/13152 publication (or record, April 1997; PTO 1449) in view of Kessler et al (of record, Demenita 6(6): 330-3, 1995; PTO 892), US Pat No. 5,429,947 (July 1995, PTO 892), Burbaea *et al* (of record, ZH Nevropatol Psikhiatr IM S Korsakova 86(1): 103-105, 1986; PTO 1449) and Jankovic et al (J Immunol 135(2 suppl): 583s-587s, Aug 1985, PTO 892).

The WO 97/13152 publication teaches a diagnostic method comprising collecting blood from a number of individuals or individual such as demented patients or healthy normal subjects, isolating platelet from the said blood samples (See entire document, page 8 in particular), collecting the platelets and preparing platelet proteins or fraction thereof by isoelectric focusing, (See page 10) wherein said proteins have a pI between 7 and 9 which anticipates the claimed pI above about 6.5 as recited in claim 6 (See page 12, Fig 4). The reference platelet protein having a pI of 9 is above the claimed pI above about 6.5 as recited in claim 8. Claims 11-13 are included in this rejection because the term "about" expands the claimed pI to read on the reference pI of the platelet proteins and the claimed platelet proteins appear to be the reference platelet proteins.

The claimed invention in claim 6 differs from the teachings of the reference only that the method of diagnosis of schizophrenia in an individual is by detecting a DTH reaction to platelet derived proteins or fractions thereof having a pI of above about 6.5.

The claimed invention in claims 7 and 9 differs from the teachings of the reference only that the method of diagnosis of schizophrenia in an individual is by detecting a DTH reaction to platelet derived proteins or fractions thereof by injecting into a subject said platelet proteins or fraction therefrom and examining the subject for the occurrence of delayed type hypersensitivity reaction at the site of injection, a positive result being a reaction above that which is observed in non-schizophrenic subjects, indicating that the subject ahs a high likelihood of being schizophrenic.

Kessler *et al* teach platelets triggers autoimmune events which are apparently involved in schizophrenia (See page 330, column 1, first paragraph, in particular) and the numbers of platelet dense granules and platelet cell size in schizophrenic patients increased compared with healthy non-schizophrenic control (See Abstract, page 331, column 2, Table 1, in particular). Kessler *et al* further teach that the number of dense bodies per platelet in schizophrenic patients is relatively the same as the Alzheimer-type demented patient (See Tables 1 and 2, in particular) and the number of dense granules in platelets from schizophrenic and demented patients are significantly higher than non-schizophrenic young individual (See Table 1 and 2, in particular).

The '947 patent teaches a method of screening schizophrenia in a subject by detecting the elevated levels of a protein such as proteins 127 and 128 having a 40,000 Mr and pI 5.7 and 5.9 respectively found in Alzheimer and schizophrenic patients (See column 7, lines 56, Fig 1, in particular). The reference pI of 5.7 and 5.9 is about the claimed pI of 6.5. The '947 patent further teach that another protein such as α-2 haptoglobin having a molecular weight of 18,000

and a pI of 6.5 that is present in increased concentration in both Alzheimer's disease and schizophrenic patients (See 7, lines 45-48, Fig 2A-B, in particular). The elevated levels of the reference proteins are found predominantly in the blood that contains platelets (See column 4, lines 13-18, in particular) and are useful as markers for diagnosis of schizophrenia and dementia in Alzheimer (See claims 1-2, in particular).

Burbaea *et al.* teach the use of delayed type hypersensitivity reaction (DTH) for a diagnostic method for schizophrenia to neurospecific proteins such as S-100 and 10-40-4 (See abstract in particular).

Jankovic *et al* teach diagnosis of schizophrenia in an individual by detecting a delayed type hypersensitivity reaction to a human brain S-100 protein and the high incidence of positive skin DTH reaction to the reference protein in schizophrenia indicates that cell-mediated immune processes may be involved in schizophrenia (See abstract, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the brain S-100 protein as taught by Burbaea *et al* or Jankovic *et al* for the platelet proteins or platelet proteins fractions having a pI of about 6.5 to 9 as taught by the WO97/13152 publication or the various proteins having a pI above about 6.5 as taught by the '947 patent because Kessler *et al* teach platelets triggers autoimmune events which are apparently involved in schizophrenia (See page 330, column 1, first paragraph, in particular). From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because Burbaea *et al* teach the use of delayed type hypersensitivity reaction (DTH) for a diagnostic method for schizophrenia (See abstract in particular). Jankovic *et al* teach that cell mediated immune mechanism which can be determine by skin delayed reaction to any self protein such as brain S-100 protein or enolase is useful for diagnosis of schizophrenia. Kessler *et al* teach platelets triggers autoimmune events which are apparently involved in schizophrenia (See page 330, column 1, first paragraph, in particular) and the numbers of platelet dense granules and platelet cell size in schizophrenic patients increased compared with healthy non-schizophrenic control (See Abstract, page 331, column 2, Table 1, in particular). Kessler *et al* further teach that the number of dense bodies per platelet in schizophrenic patients is relatively the same as the Alzheimer-type demented patient (See Tables 1 and 2, in particular). The WO 97/13152 publication teaches platelet preparation comprising proteins or fractions thereof having a pI

between 7 and 9. The '947 patent teaches elevated levels of the reference proteins such as 127, 128 and α-2 haptoglobin having a pI of about 6.5 is useful as markers for diagnosing schizophrenia and Alzheimer (See claims of '947 patent, in particular). The platelet proteins in the claimed method appear to be the same reference proteins as taught by the references having an apparent pI above about 6.5 which is within the range of above 6.5 to about 9.5 and the function of the references proteins such as inducing delayed type reaction is inherently properties of the reference proteins. Further, none of the instant claims recite a specific molecular weight associated with the claimed pI. Since the Patent Office does not have the facilities for examining and comparing the platelets proteins or fractions therefrom of the instant invention to those of the prior art, the burden is on applicant to show that the prior art proteins are different from the platelet proteins in the claimed method. See In re Best, 562 F.2d 1252, 195 USPQ 430(CCPA 1977).

Applicants' arguments filed 2/11/03 have been fully considered but are not found persuasive.

Applicants' position is that (1) Shinitzky et al relates to assays for the diagnosis of Alzheimer's type dementia and the presently pending claims relate to diagnostic methods of schizophrenia. (2) Pages 10-11 and Table 1 of the instant specification shows that 38 out of the 41 schizophrenic patients exhibited a DTH reaction while none of the 21 demented patients tested exhibited a DTH reaction. (3) Kessler et al reference does not remedy the deficiencies of the Shinitzky et al reference. In particular, Kesser et al state that the numbers of platelet dense granules and platelet cell size in schizophrenic patients increased compared to age-matched healthy controls. In contrast, the number of platelet dense granules decrease compared to healthy persons. Kessler et al merely teach measuring the number of platelet dense granules and platelet cell size to determine whether a patient is schizophrenic. (4) The Burbaea et al reference does not remedy these deficiencies. Burbaea et al relates to the body sensitization of patients to neurospecific proteins S-100 and 10-40-4 and the reference does not disclose determining schizophrenia in patient by injecting platelets into the patient and determining whether there is a DTH reaction at the site of the injection.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In instant case, The WO

97/13152 publication (Shinitzky et al) teaches a diagnostic method comprising collecting blood from a number of individuals such as demented patients or healthy normal subjects, isolating platelet from the said blood samples (See entire document, page 8 in particular), collecting the platelets and preparing platelet proteins by isoelectric focusing, (See page 10) wherein said proteins have a pI between 7 and 9 which anticipates the claimed pI above about 6.5 as recited in claim 6 (See page 12, Fig 4). The reference platelet protein having a pI of 9 is above the claimed pI above about 6.5 as recited in claim 8. Further the term "about" expands the claimed pI to read on the reference pI of the platelet proteins and the claimed platelet proteins appear to be the reference platelet proteins. Kessler *et al* teach platelets triggers autoimmune events which are apparently involved in schizophrenia (See page 330, column 1, first paragraph, in particular) and the numbers of platelet dense granules and platelet cell size in schizophrenic patients increased compared with healthy non-schizophrenic control (See Abstract, page 331, column 2, Table 1, in particular). Kessler *et al* further teach that the number of dense bodies per platelet in schizophrenic patients is relatively the same as the Alzheimer-type demented patient (See Tables 1 and 2, in particular) and the number of dense granules in platelets from schizophrenic and demented patients are significantly higher than non-schizophrenic young individual (See Table 1 and 2, in particular). Burbaea et al relates to the body sensitization of patients to neurospecific proteins S-100 and 10-40-4 and the reference does not disclose determining schizophrenia in patient by injecting platelets into the patient and determining whether there is a DTH reaction at the site of the injection. Jankovic *et al* teach diagnosis of schizophrenia in an individual by detecting a delayed type hypersensitivity reaction to a human brain S-100 protein that is also expressed in other tissue and the high incidence of positive skin DTH reaction to the reference protein in schizophrenia indicates that cell-mediated immune processes may be involved in schizophrenia (See abstract, in particular). The '947 patent teaches a method of screening schizophrenia in a subject by detecting the elevated levels of a protein such as proteins 127 and 128 having a 40,000 Mr and pI 5.7 and 5.9 respectively found in Alzheimer and schizophrenic patients (See column 7, lines 56, Fig 1, in particular). The term "about" expands the range of the pI to read on the reference pI. The '947 patent further teach that another protein such as α-2 haptoglobin having a molecular weight of 18,000 and a pI of 6.5 that is present in increased concentration in both Alzheimer's disease and schizophrenic patients (See 7, lines 45-48, Fig 2A-B, in particular). The elevated levels of the reference proteins are found predominantly in the

blood that contains platelets (See column 4, lines 13-18, in particular) and are useful as markers for diagnosis of schizophrenia and dementia in Alzheimer (See claims 1-2, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the brain S-100 protein as taught by Burbaea *et al* or Jankovic *et al* for the platelet proteins or platelet proteins fractions having a pI of about 6.5 to 9 as taught by the WO97/13152 publication or the various proteins having a pI above about 6.5 as taught by the '947 patent because Kessler *et al* teach platelets triggers autoimmune events which are apparently involved in schizophrenia (See page 330, column 1, first paragraph, in particular). From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because Burbaea *et al* teach the use of delayed type hypersensitivity reaction (DTH) for a diagnostic method for schizophrenia (See abstract in particular). Jankovic *et al* teach that cell mediated immune mechanism which can be determine by skin delayed reaction to any self protein such as brain S-100 protein or enolase is useful for diagnosis of schizophrenia. Kessler *et al* teach platelets triggers autoimmune events which are apparently involved in schizophrenia (See page 330, column 1, first paragraph, in particular) and the numbers of platelet dense granules and platelet cell size in schizophrenic patients increased compared with healthy non-schizophrenic control (See Abstract, page 331, column 2, Table 1, in particular). Kessler *et al* further teach that the number of dense bodies per platelet in schizophrenic patients is relatively the same as the Alzheimer-type demented patient (See Tables 1 and 2, in particular). The WO 97/13152 publication teaches platelet preparation comprising proteins or fractions thereof having a pI between 7 and 9. The '947 patent teaches elevated levels of the reference proteins such as 127, 128 and α-2 haptoglobin having a pI of about 6.5 is useful as markers for diagnosing schizophrenia and Alzheimer (See claims of '947 patent, in particular). The platelet proteins in the claimed method appear to be the same reference proteins as taught by the references having an apparent pI above about 6.5 or within the range of above 6.5 to about 9.5 and the function of the references proteins such as inducing delayed type reaction is inherently properties of the reference proteins. Further, none of the instant claims recite a specific molecular weight associated with the claimed pI. Since the Patent Office does not have the facilities for examining and comparing the platelets proteins or fractions therefrom of the instant invention to those of the prior art, the burden is on applicant to show that the prior art proteins are different from the

platelet proteins in the claimed method. See In re Best, 562 F.2d 1252, 195 USPQ 430(CCPA 1977).

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

14. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
May 5, 2003

Christina Chan

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600